Notice of Allowability	Application No.	Applicant(s)	
	10/814,160	WALLACH ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *10 August 2007*.

2. ☒ The allowed claim(s) is/are *1-8, 11-17, and 27*.

3. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☒ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☒ Certified copies of the priority documents have been received in Application No. *09/644,827* .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date 20070919a.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date 20040401;20060609
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☒ Interview Summary (PTO-413), Paper No./Mail Date *20070919a* .
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

2. Authorization for this examiner's amendment was given in a telephone interview with Roger L. Browdy on September 25, 2007.

3. The application has been amended as follows:

In the claims:

The following set of claims has replaced the prior set of claims submitted as part of the amendment filed July 6, 2007:

Claim 1. (Currently Amended). An isolated DNA molecule comprising a nucleotide sequence coding for a ~~purified~~ polypeptide that binds to caspase-8, said polypeptide comprising an amino acid sequence selected from the group consisting of: (a) the amino acid sequence of SEQ ID NO:6 or the amino acid sequence of SEQ ID NO:7; and (b) the amino acid sequence of an analog of (a), having no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion or insertion of an amino acid~~, which analog binds to caspase-8; (c) the amino acid sequence of a polypeptide encoded by a DNA sequence capable of hybridizing with the DNA sequence of SEQ ID NO:5 or the portion of RPCI5-I057120 which encodes SEQ ID NO:7, under moderately stringent conditions, which polypeptide binds to caspase-8~~.

Claim 2. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said polypeptide consists of ~~the polypeptide~~ an amino acid sequence of (a) or (b).

Claim 3. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said polypeptide consists of ~~the polypeptide~~ an amino acid sequence of (a).

Claim 4. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:6.

Claim 5. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO:7.

Claim 6. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said amino acid sequence of (a) is SEQ ID NO:6.

Claim 7. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, wherein said amino acid sequence of (a) is SEQ ID NO:7.

Claim 8. (Currently Amended). An isolated DNA molecule comprising a nucleotide sequence coding for a ~~purified~~ polypeptide that binds to caspase-8, said polypeptide consisting of the amino acid sequence of a fragment of SEQ ID NO:6 or a fragment of SEQ ID NO:7, which fragment binds to caspase-8.

Claims 9 and 10. (Cancelled)

Claim 11. (Currently Amended) An isolated DNA ~~sequence~~ molecule in accordance with claim 1, comprising the ~~DNA~~ nucleotide sequence of SEQ ID NO:5.

Claim 12. (Currently Amended). A vector comprising ~~a DNA~~ the nucleotide sequence of a molecule according to claim 1.

Claim 13. (Currently Amended). A vector comprising ~~a DNA~~ the nucleotide sequence of a molecule according to claim 8.

Claim 14. (Original) A eukaryotic or prokaryotic host cell containing a vector according to claim 12.

Claim 15. (Original) A eukaryotic or prokaryotic host cell containing a vector according to claim 13.

Claim 16. (Currently Amended) A method for producing a polypeptide that binds to caspase-8, said polypeptide comprising an amino acid sequence selected from the group consisting of: (a) the amino acid sequence of SEQ ID NO:6 or the amino acid sequence of SEQ ID NO:7; and (b) the amino acid sequence of an analog of (a), having no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion or insertion of an amino acid, comprising growing a host cell in accordance with claim 14 under conditions that allow production of said polypeptide, and isolating said polypeptide.

Claim 17. (Currently Amended) A method for producing a polypeptide that binds to caspase-8, said polypeptide consisting of the amino acid sequence of a fragment of SEQ ID NO: 6 or a fragment of SEQ ID NO: 7, comprising growing a host cell in accordance with claim 15 under conditions that allow production of said polypeptide, and isolating said polypeptide.

Claims 18-26. (Cancelled)

Claim 27. (Currently Amended) An isolated antisense oligonucleotide ~~comprising~~ consisting of at least [[9]] 30 nucleotides of a sequence fully complementary to ~~a DNA~~ the nucleotide sequence of a molecule according to claim 1.

Claims 28-33. (Cancelled)

In the specification:

Paragraph [0062] has been replaced with the following:

[0062] Figure 3 (a) and (b) shows the putative full length sequence of the human nucleotide (SEQ ID NO:3) and deduced amino acid sequence (SEQ ID NO:4) N-acetylglucosamine-6-phosphate deacetylase composed of the 5' extension of clone J2, the EST clone AA460869 and exon trap clone L48741.

Paragraph [0068] has been replaced with the following:

[0068] Figure 7 (a)-(e) shows the alignment of the 574 amino acids of the open reading frame derived from the deduced amino acid sequence of clone p74 (denoted cloned) compared to the 1428 amino acids of the open reading frame derived from the deduced amino acid sequence of PAC clone RPCI5-I057120 (denoted deduced).

Paragraph [0069] has been replaced with the following:

[0069] Figure 8 (a) and (b) shows the alignment of the open reading frame of the deduced amino acid sequence of PAC clone RPCI5- i057120 (top sequence) (SEQ ID

NO:8) with the sequence of histone deacetylase A (lower sequence, GENBANK accession number NP-006028.1) (SEQ ID NO:9).

Drawings

4. The following changes to the drawings have been approved by the examiner and agreed upon by applicant:

Replace Fig. 3 (3/19) with the same but labeled as "Fig. 3 (a)"; replace Fig. 3 (a) (4/19) with the same but labeled as "Fig. 3 (b)"; replace Fig. 7 (9/19) with the same but labeled as "Fig. 7 (a)"; replace Fig. 7 (a) (10/19) with the same but labeled as "Fig. 7 (b)"; replace Fig. 7 (b) (11/19) with the same but labeled as "Fig. 7 (c)"; replace Fig. 7 (c) (12/19) with the same but labeled as "Fig. 7 (d)"; replace Fig. 7 (d) (13/19) with the same but labeled as "Fig. 7 (e)"; replace Fig. 8 (14/19) with the same but labeled as "Fig. 8 (a)"; and replace Fig. 8 (a) (15/19) with the same but labeled as "Fig. 8 (b)".

5. In order to avoid abandonment of the application, applicant must make these above agreed upon drawing changes.

Election/Restrictions

6. After further consideration, the requirement to elect a single species of the invention of Group I, as set forth in section 5, beginning at page 10 of the Office action mailed January 16, 2007, has been withdrawn. Notably, the polypeptides of SEQ ID NO: 6 and SEQ ID NO: 7 comprise amino acid sequences that are substantially identical, as it appears that the polypeptides are the products of alternatively spliced transcripts of a single gene.

Examiner's Statement of Reasons for Allowance

7. The following is an examiner's statement of reasons for allowance:

The prior art does not teach or fairly suggest an isolated polypeptide that binds to caspase-8, said polypeptide comprising an amino acid sequence selected from the group consisting of: (a) the amino acid sequence of SEQ ID NO:6 or the amino acid sequence of SEQ ID NO:7; and (b) the amino acid sequence of an analog of (a), having no more than ten changes in the amino acid sequence of (a), each said change being a substitution, deletion or insertion of an amino acid; accordingly, the prior art does not teach or fairly suggest an isolated nucleic acid molecule encoding said polypeptide, a vector comprising the nucleotide sequence of said nucleic acid molecule, a host cell comprising said vector, or a method for producing said polypeptide or a fragment thereof by culturing said host cell or a host cell comprising a vector comprising a nucleotide sequence encoding said fragment.

Furthermore, inasmuch as the claims are directed to nucleic acid molecules encoding "analogs" of a polypeptide comprising the amino acid sequence of SEQ ID NO: 6 or SEQ ID NO: 7, the analog must retain the ability to bind to caspase- 8 and comprises an amino acid sequence differs from the amino acid sequences of polypeptides of SEQ ID NO: 6 or SEQ ID NO: 7 by no more than 10 amino acid substitutions, deletions, or insertions. While some of such variants of the polypeptides of SEQ ID NO: 6 or SEQ ID NO: 7 may not retain the ability to bind to caspase-8, the claimed nucleic acid molecules encode polypeptides that necessarily do so, and the Examiner finds no factual evidence teaching or reasonably suggesting that the claimed nucleic acid molecules encoding such functional polypeptides comprising amino acid sequences that are at least about 98% identical to the amino acid sequence of SEQ ID NO: 65 or SEQ ID NO: 7 could not be made after only routine and conventional experimentation. See *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) ("[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless

there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.")

In addition, though the prior art[1] teaches, for example, compositions comprising mixtures of up to 4^{15} isolated "random" 15-nucleotide DNA oligonucleotides, including in particular an oligonucleotide comprising at least 9 nucleotides of a sequence complementary to a nucleotide sequence encoding a polypeptide according to claim 1, the prior art does teach or fairly suggest an isolated oligonucleotide consisting of at least 30 nucleotides of a sequence fully complementary to the nucleotide sequence of a molecule according to claim 1.

Additionally, although U.S. Patent Application Publication No. 2001/0053519 A1 (Fodor et al.), for example, discloses arrays that comprise random oligomers of any length, including, for example, oligomers of 2, 8, and 10-25 nucleotides (see entire document; e.g., page 10, paragraph [0101]), the production of such arrays comprised of random oligomers of a size in excess of 17 nucleotides is considered prohibitive. To produce an array comprised of random oligomers of 18 nucleotides, for example, it is estimated that it would be necessary to manufacture 68,720 chips at a density of 1×10^6 oligonucleotides per chip. At the present cost of manufacturing a single chip of such density, it is estimated that it would cost $34,000,000.00 to produce the array. The present claims are directed to nucleic acid molecules of at least 30 nucleotides in length, so the cost of manufacturing a chip comprising oligonucleotides encompassed by the claims would be even more substantial.

Still, *arguendo*, if it were perhaps deemed practical and/or feasible to manufacture mixtures of longer "random" sequence oligonucleotides (e.g., at least 30 nucleotides in length), it is submitted that there would be no motivation to select members of the subgenus of oligonucleotides consisting of a sequence fully complementary to the nucleotide sequence of a molecule according to claim 1 from among the larger genus of oligonucleotides comprising disparate sequences, which are

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[1] See, e.g., Zhang et al. (*Proc. Natl. Acad. Sci. U S A.*1992 Jul 1; **89** (13): 5847-5851); entire document (e.g., the abstract).

either not complementary to the nucleotide sequence of a molecule according to claim 1, or only partially so. See *In re Baird*, 29 USPQ2d 1550 (CA FC 1994).

Support for the amendment of claim 27 to recite a limitation that the oligonucleotide consist of at least 30 nucleotides of a sequence fully complementary to the nucleotide sequence of a molecule according to claim 1 is found in the specification, as filed, at, e.g., paragraph [0212].

8. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

9. Claims 1-8, 11-17, and 27 have been allowed.

10. Claims 1-8, 11-17, and 27 have been renumbered as claims 1-16, respectively.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner
Art Unit 1643

slr
September 26, 2007